

**REMARKS**

**I. Status of the Claims**

Claims 1, 2, 7, 8, 11-18, 23-25, and 27-38 have been canceled. New claims 39-44 claims have been added. These claims correspond to the original claims of this application, therefore, support for new claims 39-45 can at least be found in original claims 1-6. Accordingly, no new matter has been added by the amendments provided herein.

**II. Rejection under 35 U.S.C. § 112, second paragraph**

Claims 1, 2, 7, 8, 11-18, 23-25, and 27-38 are rejected under 35 U.S.C § 112, second paragraph, as allegedly indefinite. Office Action, page 2. Applicant respectfully traverses this rejection for at least the following reasons.

Applicant thanks the Examiner for her suggested claim language on page 4 of the Office Action, however, Applicant respectfully declines to accept the suggested language, in part because the proposed claim is drawn to a method of producing a virus, not a method of preparing cells. Instead, Applicant has cancelled the pending claims and re-presented the original claims of this application. The return to the original claims simplifies the claim language and obviates claim language issues that may have inadvertently arisen as a consequence of prior amendments made in a good faith effort to advance prosecution. Accordingly, Applicant submits that the claims are clear and definite and respectfully requests that the Examiner withdraw the rejection.

**III. Rejection under 35 U.S.C. § 103**

Claims 1, 2, 7, 8, 11-18, 23-25, and 27 stand rejected as allegedly unpatentable over BRYAN GRIFFITHS & DENIS LOOBY, *Scale-Up of Suspension and Anchorage-Dependent Animal Cells*, in 75 METHODS IN MOLECULAR BIOLOGY: BASIC CELL CULTURE PROTOCOLS 59, 59-74 (Jeffrey W. Pollard & John M. Walker eds., 2d ed. 1997) ("Griffiths") and JEFFREY W. POLLARD, *Basic Cell Culture*, in 75 METHODS IN MOLECULAR BIOLOGY: BASIC CELL CULTURE PROTOCOLS 1, 1-11 (Jeffrey W. Pollard & John M. Walker eds., 2d ed. 1997) ("Pollard"). Office Action, page 5. The Examiner further relies upon the discussion of "Friendship Cake/Bread History" available at <http://recipecircus.com> and "Amish Friendship Bread" available at <http://en.wikipedia.org> to establish the definition and recipe of a bread calling for a starter culture. *Id.*

The Examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. M.P.E.P. § 2142. In *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 82 U.S.P.Q. 2d 1385 (2007), the Supreme Court confirmed that the "framework for applying the statutory language of §103" was still based on its landmark decision in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966). Under *Graham*, there are four factors for consideration when determining whether an invention is obvious:

- (1) the scope and content of the prior art;
- (2) the differences between the prior art and the claims at issue;
- (3) the level of ordinary skill in the art; and
- (4) secondary considerations.

383 U.S. at 17, 148 U.S.P.Q. at 467. Although the question of obviousness must be resolved on the basis of these factual determinations, the Supreme Court pointed out that there is no inconsistency between the *Graham* analysis and the idea underlying the teaching, suggestion, or motivation (“TSM”) test. *KSR*, 127 S. Ct. at 1741, 82 U.S.P.Q. 2d at 1389. Further, in its recent published revised examination guidelines, the USPTO has solidified that the TSM test is a valid rationale for determining obviousness. See M.P.E.P. § 2141.

In the outstanding Office Action, the Examiner acknowledges that neither Griffiths nor Pollard explicitly disclose that the original culture is split into at least two portions/parts. See Office Action, page 6. However, the Examiner asserts that it would be obvious to one of ordinary skill in the art to split the starter culture, using the majority of it for the production of a biological product, and retaining the subsequent portion for passage and expansion, based on the disclosure in articles titled “Friendship Cake/Bread History” and “Amish Friendship Bread.” *Id.* at page 7. Applicant respectfully disagrees and traverses this rejection for at least the following reasons.

As an initial matter, Applicant points out that all the rejected claims have been canceled and the new claims require anchorage dependent cells. The cited art does not teach or suggest the use of the claimed method with anchorage dependent cells.

Moreover, the primary references cited in the § 103 rejection, Griffiths and Pollard, disclose protocols used for preparing cell cultures. To the contrary, the secondary references, the “Friendship Cake/Bread History” and the “Amish Friendship Bread” articles only disclose a process of preparing bread. Applying the *Graham* factors, and considering the level of ordinary skill in the area of cell culture protocols,

one would not conclude that this level includes the skill of a baker. Therefore, there is no reason why one skilled in that particular art would consider applying techniques used in the process of making bread to a process for preparing cells for the production of a biological, for example, a virus. Moreover, even though the “Friendship Cake/Bread History” and the “Amish Friendship Bread” articles may disclose dividing up the starter culture into two parts, given that the process of making bread is completely unrelated to cell culture protocols, there is no way one of ordinary skill in the art would have been able to predict the results of using this technique in a process of preparing cells for the production of a biological, without the benefit of hindsight. Accordingly, Applicant submits that the Examiner has failed to establish that the claimed invention is *prima facie* in view of the cited art.

Even if the Examiner has established a *prima facie* case of obviousness, which she has not, Applicant can come forward with arguments and/or evidence to rebut the *prima facie* case. See M.P.E.P. § 2145. Rebuttal evidence may include evidence of “secondary considerations,” such as long felt but unsolved needs. See *id.*; see also *Graham v. John Deere Co.*, 383 U.S. at 17, 148 U.S.P.Q. at 467.

The production of biologicals on cell lines requires the preparation of large amounts of cells using a scaling up procedure in bioreactors. Typically, continuous processes are used for scaling up a cell culture population in the context of producing a biological. See Applicant’s specification at page 3, lines 20-23. First, cells are grown in a first bioreactor, and after a certain cell density is reached, the cells are fed continuously from the first bioreactor into a second bioreactor. *Id.* at lines 24-25. In this second bioreactor, viruses are grown on the cells and subsequently these viruses are

withdrawn continuously from this second bioreactor. *Id.* at lines 25-27. Generally, these types of preparation procedures are very time consuming and necessitate the operation of a large number of bioreactors for the preparation of the cells as well as for the production of the biologicals. See *id.* at page 1, lines 29-32. Thus, there has been a long-felt need for a faster and more efficient process.

Applicant has met this need by inventing a new and faster process for scaling up a cell culture for the production of a biological, wherein the cells are anchorage dependent cells. Unlike continuous scaling up procedures, Applicant's claimed method uses a discontinuous process. See Applicant's specification at page 2, lines 1-15. In embodiments of the claimed invention, cells are cultured to produce a preproduction batch, and then the cells of the preproduction batch are divided into two parts. See *id.* at page 2, lines 1-15. The first part, approximately 80-90% of the cells, is used to prepare a culture of cells to grow a biological such as a virus for a vaccine. *Id.* at page 2, lines 4-5 and 27-28. The second part, approximately 10-20% of the preproduction batch, is used as a seed for at least one additional batch not immediately used for the production of any biological product. See *id.* at page 2, lines 6-7 and 30-32. The cells of the second part of the preproduction batch can be expanded to a greater cell population for the preparation of at least one subsequent preproduction batch. See *e.g., id.* at page 6, lines 15-16. Thus, using Applicant's claimed method, a vaccine manufacturer, for example, can rapidly produce vaccine without waiting for all preproduction batches to reach full maturity. See Applicant's specification at page 3, line 35 to page 4, line 2.

As discussed above, the Examiner asserts that it would have been obvious to one of ordinary skill in the art to split the starter culture in the process of producing a biological, using the majority of it for the production of a biological product, and retaining the subsequent portion for passage and expansion, based on the disclosure in articles titled "Friendship Cake/Bread History" and "Amish Friendship Bread." See Office Action at page 7. According to the "Friendship Cake/Bread History" article, the recipe for making Amish friendship bread or similar breads in which the starter cultures are split into two portions have been around for more than 100 years. In view of the need for a faster and more efficient process, if it was so obvious to use techniques associated with bread making, i.e., splitting a starter culture into two portions, in a process for scaling up a cell culture population for producing a biological, as asserted by the Examiner, then why didn't someone arrive at this combination prior to Applicant's filing date.

The fact of the matter is, prior to Applicant's claimed invention no one considered splitting the preproduction batch (starter culture) used in the production of a biological into two parts. Prior to Applicant's claimed invention, cells for use in the production of a biological were only produced using a continuous process in which the entire preproduction batch was used for preparing a biological. As discussed above, this continuous process was slow and necessitated a number of bioreactors for the preparation of cells as well as for the production of the biologicals. Recognizing this long-felt need in the industry, Applicant invented a method for the preparation of cells for use in the production of a biological comprising a discontinuous process in which the preproduction batch was divided into two parts: a first part used for the production of a biological and a second part used as a seed for the preparation of at least one

subsequent preproduction batch. By splitting the preproduction batch into two parts, Applicant's claimed method provides a faster and more efficient process for scaling up a cell culture for the production of a biological. Thus, Applicant's claimed method satisfied a long-felt, but unsolved need in the industry, which is evidence that rebuts any *prima facie* case of obviousness based on the cited references.

In view of the above, Applicant respectfully requests that the Examiner reconsider and withdraw the foregoing § 103 rejection.

**IV. Conclusion**


In view of the foregoing amendments and remarks, Applicant respectfully requests reconsideration of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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